ESF EMRC Workshop:

CARDIOVASCULAR GENOMICS: NEW PATHOPHYSIOLOGICAL CONCEPT

Maastricht, Netherlands, 30 November - 2 December 2001

Executive summary

Four years ago - in December 1997 - the first European Science Foundation Workshop on Cardiovascular Specific Gene Expression was held in Maastricht. The progress in the field in the four years until December 2001 has been spectacular. In 1997, gene expression was still an art focused on individual genes; in 2001, many labs have access to microarray facilities to determine the expression of thousands of genes simultaneously. In 1997, gene expression was an area of fundamental research in basic molecular biology laboratories; in 2001, clinical cardiovascular research has incorporated gene expression approaches. In 1997, the interpretation of a gene expression experiment was usually straightforward; in 2001, advanced bioinformatics tools are used to interpret the extreme complexities of genetic control of cell and tissue function.

The second symposium of this series was focused on cardiovascular genomics: new pathophysiological concepts. The organizing committee chose to invite a group of renowned scientists and young investigators around four topics of eminent importance in cardiovascular research. The topics reflect the major present-day clinical cardiovascular problems: atherosclerosis, hypertension, arrhythmias and heart failure. In addition to these four disease-driven topics, the workshop had sessions on gene expression methodologies and cellular transplant approaches to cardiovascular disease.

In the opening session, dr. E. Olson from Dallas gave a brilliant review on transcriptional regulation of cardiac development and hypertrophy. The atherosclerosis session contained in-depth presentations on gene expression analysis in the vessel wall and the plaque. Several groups of genes related to phenomena like cell growth and apoptosis, matrix structure and cell-cell connection now emerge as vital in the process of atherosclerosis. The hypertension session also had a focus on the vessel wall. Developmental aspects, endothelial function and cell signaling pathways were reviewed by the speakers in this session.

The two sessions devoted to cardiac aspects covered gene expression pathways involved in arrhythmias, hypertrophy and failure. A particular focus was given to the role of contractile proteins. The arrhythmia session reviewed the gene expression of various ion channels.

The session of gene expression analysis provided a didactic overview of the major methodological approaches used in gene expression analysis. Finally, a series of lectures was devoted to the use of cellular therapies to improve cardiac function. This novel area of research offers exciting perspectives for therapeutic applications.

The whole meeting offered science at the highest possible level. The formula of the workshop - limited participation, mix of established and young investigators, international, predominantly European speakers, extensive discussion periods - was ideally suited for its highly ambitious purposes.
Future direction

The expected impact of the meeting will depend on new European collaborative initiatives. Some collaborations have already been set up after three months. This is especially true for exchange of animal models and genomic analysis in the places where the systems are up and running. This will save time and money and lead to interpretable results faster. It was obvious that the general feeling at the meeting was that genomics and proteomics are crucial tools for understanding the genome. However, the rate limiting step for fast genetic and genomic analysis is the physiomic approach. Several institutes have some techniques for functional analysis, but few have them all, which leads to incomplete phenotypic analysis. Investments and improvements in the infrastructure to perform physiomic analysis more efficient would be the way to go.

Pieter A. Doevendans
Harry Struijker Boudier
List of participants:

Babiker, F
Department of Cardiology
P.O. Box 5800
6202 AZ Maastricht
The Netherlands

Barth, A
Klinikum Grosshadern, Medizinishce Klinik
81366 Munchen
Germany

Bianchi, Dr. G.
Ospedale San Raffaele
Universita “Vita Salute”
Via Olgettina 60
20132 Milan
Italy
Bianchi.giuseppe@hsr.it

Bilsen, P
Medtronic Bakken Research Center
P.O. Box 1220
6201 MP Maastricht
The Netherlands

Bierhuizen, M
University Medical Center Utrecht
Department of Medical Physiology
Universiteitsweg 100
3584 CG Utrecht
The Netherlands

Van Bilsen, M
Department of Physiology
Cardiovascular Research Institute
Maastricht
P.O. Box 616
6200 MD Maastricht
The Netherlands

V/d Borne, S
Stationstraat 48
6221 BR Maastricht
The Netherlands

Van der Bosch, B
P.O. Box 5800
6202 AZ Maastricht
Maastricht
The Netherlands

Bruggeman, Mw. C.
AZM
Department of Microbiology
P.O. Box 5800
6202 AZ Maastricht
The Netherlands

De Bruin, T
P.O. Box 616
6200 MD Maastricht
The Netherlands

Brundel, B
Academisch Ziekenhuis Groningen
Postbus 30001
9700 RB Groningen
The Netherlands
b.j.m. brundel@med.rug.nl

Buermans
V/d Borchorststraat 7
1081 BT Amsterdam
The Netherlands

Cleutjens, K
P.O. Box 616
6200 MD Maastricht
The Netherlands

Cockx, E
Porter, Dr. G.
3160 Porter Drive
Palo Alto
California 94304
USA

Cohen Tervaart, J
Afd. Immunologie
P.O Box 616
6200 MD Maastricht
The Netherlands
Conrath, C  
Dep. of Cardiology UMC Room E03.406  
P.O. Box 85500  
3508 GA Utrecht  
The Netherlands

Corvol, Dr. P.  
College de France  
Pathologie Vasculaire et Endocrinologie Renale  
Chaire de Medicine Experimentale  
3, Rue D’Ulm  
F- 75005 Paris  
France

Creemers, E  
P.O. Box 616  
6200 MD Maastricht  
The Netherlands

Daemen, Prof. Dr. M.  
Pathology  
P.O. Box 616  
6200 MD Maastricht  
The Netherlands

Dieijen, M  
AZM klinische chemie  
P.O. Box 5800  
6202 AZ Maastricht  
The Netherlands

J-F. Dierick  
Laboratoire de Biochimie et Biologie Cellulaire  
Facultes Universitaires Notre Dame de la Paix 61  
Rue de Bruxelles  
5000 NAMUR, Belgium

Dominiczak, Dr. A.  
Gardiner Institute  
Department of Medicine and Therapeutics Western Infemary  
Glasgow G- 11 6 NT  
United Kingdom

Donahue, Dr. K.  
Department of Medicine  
Johns Hopkins University School of Medicine  
N. Wolfe St. Baltimore  
MD 21287  
USA  
Kdonahue@jhmi.edu

Fukuda, Dr. Keiichi  
Keio University  
School of Medicine  
35 Shinanomachi  
Shinjuku-ku Tokyo  
160-8582, Japan  
kfukuda@mc.keio.ac

Geurts, J  
Universiteitssingel 50  
6200 MD Maastricht  
The Netherlands

Golde, J  
P.O. box 616  
6200 MD Maastricht  
The Netherlands

Gorgels, A  
Dept. of Cadiology  
P.O. Box 5800  
6202 AZ Maastricht  
The Netherlands

Hofker, Prof. Dr. M.  
Moleculaire Genetica  
P.O Box 616  
6200 MD Maastricht  
The Netherlands

Horrevoets, Dr. H.  
AMC  
Meibergdreef 9  
1105 AZ Amsterdam  
The Netherlands  
A.J.Horrevoets@amc.uva.nl
Huynen, Dr. H.
Biocomputing Group, EMBL
P.O. Box 10.2209
69012 Heidelberg
Germany

Kääb, Dr.med. Stefan
Klinikum Grosshadern, Medizinische Klinik
81366 München
Germany
Stefan.Kaeaeb@med1.me

Kitslaar
Postbus 5800
6202 AZ Maastricht
The Netherlands

Kockx, Dr. M.
Department of Pathology
A.Z. Middelheim
Lindendreef 1
B-2020 Antwerp
Belgium

Lamas, Dr. S.
CIB/CSIC
Velazquez 144
28006 Madrid
Spain
Slamas@fresno.csic.es

De Leeuw, Prof. Dr. P.
Interne Geneeskunde
P.O Box 616
6200 MD Maastricht
The Netherlands

Lembo, Dr. G.
Associat Professor of Internal Medicine
Dept. of Experimental Medicine & Pathology
“La Sapienza” University of Rome
c/o IRCCS NEUROMED
Loc. Camerelle
86077 Pozzilli (IS)
ITALY
Lembo@neuromed.it

Mairahu
AMC Amsterdam
Meibergdreef 9
1105 AZ Amsterdam
The Netherlands

De Mey, J
P.O. Box 5800
6202 AZ Maastricht
The Netherlands

Michiels, Dr. C.
Laboratoire de Biochimie et Biologie Cellulaire
Facultes Universitaires Notre Dame de la Paix
61, Rue de Bruxelles
5000 Namur
Belgium
Caline.michiels@fundp.ac.be

Montfrans, G
Meibergdreef 9
1105 AZ Amsterdam Z.O
The Netherlands

Mummery, Mw. C.
NIOB
Uppsalalaan 8
3584 CT Utrecht
The Netherlands

Nabauer, Dr. M.
Klinikum Grosshadern, Medizinische Klinik
81366 München
Germany

Olson, Dr. E.
Department of Molecular Biology
University of Texas Southwestern Center
6000 Harry Hines Boulevard
75390 Dallas, TX
USA
Eolson@hamon.swmed.edu
Van Onna, M
Postbus 5800
6202 AZ Maastricht
The Netherlands

Opthoff, T
Department medical physiology
University Medical Center
P.O. Box 19008
3501 DA Utrecht
The Netherlands

Pannekoek, H
AMC
Department of Biochemistry Rm. KL –161
Meibergdreef 15
1105 AZ Amsterdam
The Netherlands

Paquay, J
Bellefleur 22
6245 PK Eysden
The Netherlands

Porter, Dr. G.
3160 Porter Drive
Palo Alto
California 94304
USA

Prinzen, F
psychologie
UM
P.O Box 616
6200 MD Maastricht
The Netherlands

Ramaeckers, C
AMC
Meibergdreef 9
1105 AZ Amsterdam
The Netherlands

Ravens Prof. Dr. med. Ursula
Institut für Pharmakologie und
Toxikologie
Universitätsklinikum Carl-Gustav-Carus
Technische Universität Dresden
Karl-Marx-str. 3
01109 Dresden
Germany

Rockman, Dr. H.
Associate Professor of Medicine and Cell
Biology
Duke University Medical Center
DUMC 3104
CARL Building, Rm. 226
Durham, NC 27710
USA
Rockm001@mc.duke.edu

Rooy, E
P.O. Box 5800
6202 AZ Maastricht
The Netherlands

Rossier, B
Institut de Pharmacologie et de
Toxicologie
Universite de Lausanne
Bugnon 27, CH-1005-Lausanne
Switzerland
Bernard.Rossier@ipharm.unil.ch

Van de Schans, V
Kloterstraat 17
3950
Kavlille-Bocholt
Belgium

Schiffers, P
UM
P.O Box 616
6200 MD Maastricht
The Netherlands
P.Schiffers@Farmaco.UNIMAAS.NL
Schoenmakers, M  
Dept. of Cardiology  
P.O. Box 5800  
6202 AZ Maastricht  
The Netherlands

Schwartz, S  
Department of Pathology  
P.O. Box 357335  
University of Washington  
SEATTLE 98195-7335  
United States

Simonides  
University of Amsterdam  
Van der Boechorststraat 7  
1081 BT Amsterdam  
The Netherlands

Smits, J  
Universiteit Maastricht  
Dept. of Pharmacology and Toxicology  
P.O. Box 616  
6200 MD Maastricht

Smits, Dr. P.  
AZR-Dijkzigt  
Department of Cardiology  
P.O. Box 2040  
3000 CA Rotterdam  
The Netherlands

Sommerschild, H  
Karolinka Hospital  
Craforot Laboratory L6:00  
17176 Stockholm  
Sweden  
Hilchents@hotmail.com

Prof. Struijker Boudier  
AZM  
P.O. Box 5800  
6202 AZ Maastricht  
The Netherlands

Sussman, Dr. M.  
The Childrens Hospital and Research Foundation  
Division of Molecular Cardiovascular Biology  
3333 Burnet Avenue  
Cincinnati OH 45229-3039  
Sussman@heart.chmcc.or

Van Suylen, R  
Pathologie  
UM  
P.O Box 616  
6200 MD Maastricht  
The Netherlands

Teunissen, B  
AIO afd. Medische Fysiologie  
UMC Utrecht  
Universiteitsweg 100  
3584 CG Utrecht  
The Netherlands

Valen, Dr. G.  
Grafoordlaboratory of Experimental Surgery  
Karolinska Hospital L6:00  
S-17176 Stockholm  
Sweden

Vanderkeilen, C  
Victor de Stuersstraat 24  
6217 KS Maasticht  
The Netherlands

Van der Velden  
Department of Sportfysiology  
P.O. Box 85500  
3508 GA Utrecht  
The Netherlands

Vink, C  
P.O. Box 5800  
6202 AZ Maastricht  
The Netherlands
Country of Origin Statistics:

- The Netherlands: 40
- Germany: 5
- Switzerland: 1
- Italy: 2
- Spain: 1
- USA: 7
- France: 2
- Belgium: 4
- UK: 1
- Japan: 1
- Sweden: 2
FINAL PROGRAMME

NOVEMBER 29

Introsession
Chairman P. Doevendans

18.30 Welcome: Prof. H. Struijker Boudier

18.40 Cardiovascular disease: the clinical problems: Prof. H.J. Wellens

19.00 Transcriptional regulation: E. Olson

20.15 DINNER (castle Vaeshartelt)

NOVEMBER 30

Please note that all speakers have 25 minutes for the presentation and 5 minutes discussion

SESSION 1 08.00-09.55
Gene expression analysis
Chairman M. Hofker

08.00 Microarray: G. Porter

08.30 SAGE: B. Rossier

09.00 Proteomics: C. Michiels

09.30 Bioinformatics: M. Huynen

10.00 Coffee break

SESSION 2 10.30-12.25
Genomics and pathophysiology of atherosclerosis
Chairman M. Daemen

10.30 Micro-arrays to unravel atherosclerosis: S. Schwartz

11.00 In vitro-in vivo gene analysis: A. Horrevoets

11.30 Gene expression and plaque complexity: M. Daemen

12.00 The role of apoptosis in atherosclerosis progression: M. Kockx

12.30 LUNCH
SESSION 3  14.00-16.25  
Genomics and hypertension  
Chairman P. de Leeuw  
14.00  Disease complexity: P. Corvol  
14.30  Predisposition for hypertension: analysis of candidate genes G. Bianchi  
15.00  Vascular gene transfer/therapy: from animals to humans: A. Dominiczak  
15.30  Hormones and signalling pathways: G. Lembo  
16.00  Endothelial changes in hypertension: S. Lamas  
19.00  Bustransport Castle Vaeshartelt to Castle Neercanne for DINER

DECEMBER 1

SESSION 4  08.00-09.55  
Gene expression in cardiac hypertrophy and failure  
Chairman P. Doevendans  
08.00  Microarrays and cardiac tissue: H. Smeets  
08.30  Ca handling proteins: H. Rockman  
09.00  Adaptation of contractile proteins: M. Sussman  
09.30  Cardiac Signalling Pathways: L. de Windt  
10.00  Coffee break

SESSION 5  10.30-12.55  
Molecular remodelling in arrhythmias  
Chairman M. Nabauer  
10.30  Ion channel regulation: from genes to channels to arrhythmias: K. Donahue
11.00  Differential expression and regulation of delayed rectifier channels:  
       M. Vos

11.30  Ion channel polymorphisms and their role in ventricular arrhythmogenesis: S.  
       Kaab

12.00  Altered gene expression in atrial fibrillation: B. Brundel

12.30  G-protein 3 subunit polymorphism and atrial fibrillation:  
       U. Ravens

13.00  LUNCH

SESSION 6  14.30-16.25  
Cellular transplant  
Chairman: L. Field

14.30  Genetic modification of stemcells: T. de Vries

15.00  Human Embryonic stemcells: C. Mummery

15.30  Bone marrow derived cardiomyocytes: K. Fukuda

16.00  Cellular Cardiac reinforcement: P. Smits